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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MYERS, CARLA J	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/836,697	SIFFERT, WINFRIED	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the amendment filed February 10, 2003. Claim 37 is pending and claims 1-36 have been cancelled. Applicant's arguments and amendment set forth in the response of February 10, 2003 have been fully considered but are not persuasive to overcome all grounds of rejection. All rejections not reiterated herein are hereby withdrawn. This action is made final.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 37 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for identifying human subjects having an increased likelihood of having hypertension wherein the methods comprise detecting the presence of a C to T polymorphism at position 825 (C825T) of the gene encoding the human G protein B_3 subunit, does not reasonably provide enablement for methods of detecting the C825T polymorphism as indicative of any disease in any organism. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claim 37 as amended is drawn to a method for establishing a risk of developing a disorder associated with a substitution of a C for a T at position 825 in the G protein

B3 subunit (GNB3) of SEQ ID NO: 1. The specification teaches only a single polymorphism in the gene encoding the human G protein B_3 subunit, i.e. the polymorphism of a C to T at position 825 of the human G protein B_3 subunit of SEQ ID NO: 1. The specification reviews the results of a study in which the occurrence of the C825T polymorphism was compared in normal and hypertensive human subjects and concludes that the C825T polymorphism is more prevalent in hypertensive subjects as compared to controls. The specification is not enabling for the invention as it is broadly claimed for the following reasons: Firstly, claim 37 as broadly written includes methods for diagnosing any disease or any disorder associated with G protein dysregulation. However, the specification has identified only one disorder, i.e. hypertension, associated with the polymorphism of a C to T at position 825 of the GNB3 gene. No results are presented regarding an association between this polymorphism and the occurrence of any other disease. The post-filing date art corroborates the unpredictability in the art of establishing a correlation between the C825T polymorphisms and increased susceptibility to diseases, including diseases associated with G protein dysfunction. For example, Fogarty (Diabetologia (1998) 31:1304-1308) states that "we have found no evidence for a role of the GNB3 C825T functional variant in the genetic susceptibility to diabetic nephropathy in Type I diabetes, as assessed in a large case-control and family based association study. In addition, there appears to be no significant effect of this polymorphism on variation in blood pressure in this Type I diabetic group" (page 1308). Town (American Journal of Medical Genetics (1998) 88:465-468) reported that the C825T polymorphism is not associated with risk for

Alzheimer's Disease. Haase (Neuroscience Letters 2002. 330: 293-295) teaches that the GNB3 C825T polymorphism is not associated with MS. Kunugi et al (Journal of Neural Transmission (2002) 109: 213-218) teaches that the C825T polymorphism is not associated with schizophrenia or mood disorders. Benjafield (International Journal of Obesity (2001) 25: 777-780) teaches that the C825T polymorphism of GNB3 is not associated with overweight or obesity. Gao teaches that the GNB3 gene appears to be involved in canine cone disease. The reference teaches screening human patients with inherited retinal disease for the presence of mutations in the GNB3 gene. Four mutations were identified in the GNB3 gene, including the C825T mutation. However, Gao teaches that no mutations in the GNB3 gene were found to be associated with the occurrence of inherited retinal degeneration. Secondly, the specification teaches only the presence of a single C825T polymorphism in the human GNB3 gene. This mutations has not been identified in the GNB3 genes of other organisms and no association has been established between this GNB3 mutation and the occurrence of disease in non-human animals. Again, extensive experimentation would be required to analyze the GNB3 gene sequences of other organisms and to determine if this mutation is associated with any particular disease in these organisms. The specification does not provide specific guidance as to any specific diseases in other organisms that would be expected to be associated with the C825T mutation in the GNB3 gene. As stated in *Vaek* (20 USPQ2d 1438), the "specification must teach those of skill in the art how to make and how to use the invention as *broadly* as it is claimed" (emphasis added). The amount of guidance needed to enable the invention is related to the amount of

knowledge in the state of the art as well as the predictability in the art. *In re Fisher* 427 F. 2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Predictability or lack thereof in the art refers to the ability of one of skill in the art to extrapolate the disclosed or known results to the invention that is claimed. If one of skill in the art can readily anticipate the effect of a change in the subject matter to which the claimed invention is directed, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change in the subject matter to which the claimed invention is directed, then there is unpredictability in the art". With respect to the present invention, one cannot readily anticipate what diseases other than hypertension are associated with the C825T mutation in humans. Furthermore, one cannot readily anticipate whether the C825T is present in other organisms and is correlated with disease. In view of the high level of unpredictability in the art and the lack of guidance provided in the specification, undue experimentation would be required for one of skill in the art to practice the invention as it is broadly claimed.

RESPONSE TO ARGUMENTS:

In the response filed February 10, 2003, Applicants argue that the specification has enabled the full scope of the claimed invention. Applicants assert that in order to practice the invention of claim 37, a skilled artisan simply has to check to see whether a disorder is associated with the C825T mutation. Applicants further argue that the skilled artisan would expect that diseases in addition to hypertension will be associated with the C825T mutation.

Applicant's arguments have been fully considered but are not persuasive to overcome the present grounds of rejection. Case law has established that the specification should teach one of skill in the art how to make and use the invention as broadly as it is claimed (*Vaek* 20 USPQ2d 1438). However, in the instant application, the specification has not fulfilled this requirement because the specification has not adequately taught one of skill in the art how to identify additional diseases associated with the C825T mutation without undue experimentation. As discussed in the above rejection, the skilled artisan cannot readily determine which additional diseases would be expected to be associated with the C825T mutation. The specification has not established that any particular group of diseases would be predictably associated with the C825T mutation or the specification has not taught any particular mechanism by which the mutation acts to cause disease. Thereby, one of skill in the art is left to randomly analyze any possible disease in humans and other organisms to determine if the disease in question is associated with the C825T mutation. Such random experimentation is considered to be undue. Additionally, the post-filing date art corroborates the unpredictability in identifying additional diseases associated with the C825T mutation. As set forth in the above rejection, the art teaches that researchers have determined that the C825T mutation is NOT associated with diabetic nephrology in type 1 diabetes, Alzheimer's disease, multiple sclerosis, schizophrenia, mood disorders, overweight or obesity in humans, or inherited retinal degeneration in dogs. Accordingly, in view of the fact that the specification teaches an association between the C825T mutation and only one member, i.e., hypertension, within the broadly claimed genus of

diseases and in view of the high level of unpredictability in the art, it is maintained that undue experimentation would be required to practice the invention as it is broadly claimed.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 37 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,242,181. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of '181 are inclusive of methods which diagnose hypertension by detecting the presence of the C825T GNB3 polymorphism.

RESPONSE TO ARGUMENTS:

In the response filed February 10, 2003, Applicants request that the rejection be held in abeyance until allowable subject matter is obtained. However, the Patent Office does not hold rejections in abeyance. Accordingly, the rejection is maintained for the reasons of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (703) 308-2199. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703)-308-1119. Papers related to this application may be faxed to Group 1634 via the PTO Fax Center using the fax number (703)-872-9306 or (703)-872-9307 (after final).

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Carla Myers
August 12, 2003